WEST Search History

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DATE: Thursday, April 29, 2004

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT; PLUR=YES; OP=ADJ	
☐	L17	L16 and l10	40
☐	L16	20011206	58
☐	L15	L14 and (dna or cdna or nucleic acid or polynucleotide or nucleotide or vector or plasmid)	102
☐	L14	L13 and (mak$7 or synthe$7 or produ$7 or ferment$7 or cultur$7)	106
☐	L13	L12 and microorganism	106
☐	L12	L11 and mevalonate	176
☐	L11	(isopentenyl pyrophosphate) or (Isopentenyl diphosphate) or (methyl pyrophosphate) or (methyl trihydrogen pyrophosphate) or (butenyl pyrophosphate)	372
☐	L10	L9 or l8 or l7 or l6 or l5 or l4 or l3 or l2 or l1	30011
☐	L9	(536/23.2)!.ccls.	10802
☐	L8	(435/320.1)!.ccls.	23412
☐	L7	(435/252.3)!.ccls.	8102
☐	L6	(435/232)!.ccls.	440
☐	L5	(435/194)!.ccls.	1507
☐	L4	(435/189)!.ccls.	1204
☐	L3	(435/183)!.ccls.	4483
☐	L2	(435/132)!.ccls.	215
☐	L1	(435/41)!.ccls.	675

END OF SEARCH HISTORY

h e b b cg b chh e f c e cf

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=> d his

     (FILE 'HOME' ENTERED AT 09:09:11 ON 29 APR 2004)

     FILE 'REGISTRY' ENTERED AT 09:09:17 ON 29 APR 2004
L1             1 S ISOPENTENYL PYROPHOSPHATE/CN
L3           257 S MEVALONATE

     FILE 'HCAPLUS' ENTERED AT 09:11:41 ON 29 APR 2004

     FILE 'REGISTRY' ENTERED AT 09:11:45 ON 29 APR 2004
                 SET SMARTSELECT ON
L4            SEL L1 1- CHEM :       5 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 09:11:45 ON 29 APR 2004
L5          1182 S L4
L6             8 S L5 (L) MEVALON? (L) PREP/RL
L7             6 S L6 AND PD<20011206
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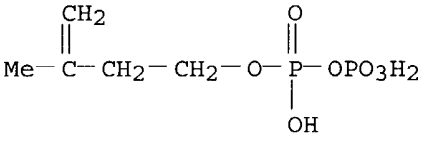
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 358-71-4 REGISTRY
CN Diphosphoric acid, mono(3-methyl-3-butenyl) ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-ol, 3-methyl-, pyrophosphate (6CI)
CN 3-Buten-1-ol, 3-methyl-, trihydrogen pyrophosphate (7CI, 8CI)
OTHER NAMES:
CN Δ3-Isopentenyl pyrophosphate
CN 3-Methyl-3-butenyl pyrophosphate
CN Isopentenyl diphosphate
CN **Isopentenyl pyrophosphate**
FS 3D CONCORD
MF C5 H12 O7 P2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, IPA, MEDLINE, NIOSHTIC, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

513 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
515 REFERENCES IN FILE CAPLUS (1907 TO DATE)
22 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d ibib ab 1-6

L7 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:612949 HCAPLUS
DOCUMENT NUMBER: 139:226151
TITLE: Development of methodology for biochemical and biosynthetic studies of isoprenoid compounds using perdeuterated mevalonate
AUTHOR(S): Eguchi, Tadashi; Dekishima, Yasumasa; Matsushima, Yoshitaka; Tamegai, Hideyuki; Kakinuma, Katsumi; Takagi, Motoki; Kuzuyama, Tomohisa; Seto, Haruo; Misawa, Norihiko; Hamano, Yoshimitsu; Dairi, Tohru
CORPORATE SOURCE: Department of Chemistry and Materials Science, Department of Chemistry, Tokyo Institute of Technology, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (**2001**), 43rd, 7-12
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Isoprenoids are chemical diverse in nature, ubiquitous in living organisms, and crucial in biol. processes. The biosynthesis of such isoprenoids proceeds through mevalonate and nonmevalonate pathways depending upon organisms and cellular organelle, isopentenyl diphosphate (IPP) being a key intermediate in both cases. Metabolic engineering and control of these pathways should thus provide new opportunity to study intriguing chemical and biochem. involved and to develop selective chemotherapeutic agents and isoprenoid-related materials. We describe a new practical approach to the preparation of highly- and multiply deuterated isoprenoids, zeaxanthin and diterpene antibiotic terpentecin being as examples, and its potential for analyzing the biosynthetic mechanism of isoprenoids, based on the metabolic engineering of microorganisms. Obviously, deuterium-labeled compds. are invaluable in biochem., bioorg. as well as physicochem. research. Metabolically engineered E. coli DK223 (pTMV20, pACCAR25ΔcrtX) produces zeaxanthin under the presence of mevalonate. Fully deuterated mevalonolactone-d9 (MVL-d9), which had been synthesized, was supplemented to the culture of the above triply-engineered E. coli, and the biosynthesized zeaxanthin was extracted and purified by repeated chromatog. All the zeaxanthin formed was proved to be derived only from the supplemented MVL-d9. This was the first example of such highly and multiply deuterated zeaxanthin, and clearly demonstrated significant potential of the present approach for the preparation of various isotope-labeled isoprenoids. Addnl. example of this approach was also demonstrated in the mechanistic study of cyclization reaction in the biosynthesis of diterpene antibiotic terpentecin. Straightforward stereochem. anal. of isoprenoid biosynthesis was demonstrated by one-shot labeling of MVL-d9 and 1H NMR spectroscopy. Precise anal. of the simplified proton spectra of highly deuterated isoprenoids, especially under the deuterium decoupled conditions, appeared to be beneficial for mechanistic enzymol., particularly, for the key transformation involving proton attack and proton quench as observed in the terpene cyclase reactions.

L7 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:435280 HCAPLUS
DOCUMENT NUMBER: 135:41836
TITLE: A gene cluster for the mevalonate pathway from Streptomyces sp. strain CL190 and use in isoprenoid synthesis
INVENTOR(S): Seto, Haruo; Kuzuyama, Tomohisa; Takahashi, Shunji; Takagi, Motoki
PATENT ASSIGNEE(S): Japan

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042476	A1	20010614	WO 2000-JP8620	20001206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001161370	A2	20010619	JP 1999-348375	19991208 <--

PRIORITY APPLN. INFO.: JP 1999-348375 A 19991208

AB A gene cluster for the mevalonate pathway enzymes, Phosphomevalonate kinase, Diphosphomevalonate decarboxylase, Mevalonate kinase, 3-Hydroxy-3-methylglutar yl CoA reductase, and 3-Hydroxy-3-methylglutar yl CoA synthase, from Streptomyces is disclosed. Recombinant expression, and use in biosynthesis of isoprenoid compds., ubiquinone, vitamin K2, or carotenoid, are claimed. A biosynthetic 3-hydroxy-3-methylglutaryl CoA reductase (EC 1.1.1.34), the rate-limiting enzyme of the mevalonate pathway for isopentenyl diphosphate biosynthesis, had previously been purified from Streptomyces sp. strain CL190 and its corresponding gene (hmgr) had been cloned. Sequence anal. of the flanking regions of the hmgr gene revealed 5 new open reading frames, orfA to -E, which showed similarity to those encoding eukaryotic and archaebacterial enzymes for the mevalonate pathway. Feeding expts. with [1-13C]acetate demonstrated that Escherichia coli JM109 harboring the hmgr gene and these open reading frames used the mevalonate pathway under induction with iso-Pr β-D-thiogalactopyranoside. This transformant could grow in the presence of fosmidomycin, a potent and specific inhibitor of the nonmevalonate pathway, indicating that the mevalonate pathway, intrinsically absent in Escherichia coli, is operating in the E. coli transformant. The hmgr gene and orfABCDE are thus unambiguously shown to be responsible for the mevalonate pathway and to form a gene cluster in the genome of Streptomyces sp. strain CL190. Production of Isopentenyl pyrophosphate (IPP) and ubiquinone was demonstrated in transformed E. coli.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:77831 HCAPLUS
DOCUMENT NUMBER: 135:164538
TITLE: Escherichia coli engineered to synthesize isopentenyl diphosphate and dimethylallyl diphosphate from mevalonate: a novel system for the genetic analysis of the 2-C-methyl-D-erythritol 4-phosphate pathway for isoprenoid biosynthesis
AUTHOR(S): Campos, Narciso; Rodriguez-Concepcion, Manuel; Sauret-Gueto, Susanna; Gallego, Francesca; Lois, Luisa-Maria; Boronat, Albert
CORPORATE SOURCE: Department de Bioquimica i Biologia Molecular, Facultat de Quimica, Universitat de Barcelona, Barcelona, 08028, Spain
SOURCE: Biochemical Journal (**2001**), 353(1), 59-67
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isopentenyl diphosphate (IPP) and its isomer dimethylallyl diphosphate (DMAPP) constitute the basic building block of isoprenoids, a family of compds. that is extraordinarily diverse in structure and function. IPP and DMAPP can be synthesized by two independent pathways: the mevalonate pathway and the recently discovered 2-C-methyl-D-erythritol 4-phosphate (MEP) pathway. Although the MEP pathway is essential in most eubacteria, algae and plants and has enormous biotechnol. interest, only some of its steps have been determined We devised a system suitable for the genetic anal. of the MEP pathway in Escherichia coli. A synthetic operon coding for yeast 5-diphosphomevalonate decarboxylase, human 5-phosphomevalonate kinase, yeast mevalonate kinase and E. coli isopentenyl diphosphate isomerase was incorporated in the chromosome of this bacterium. The expression of this operon allowed the synthesis of IPP and DMAPP from mevalonate added exogenously and complementation of lethal mutants of the MEP pathway. We used this system to show that the ygbP, ychB and ygbB genes are essential in E. coli and that the steps catalyzed by the products of these genes belong to the trunk line of the MEP pathway.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:911403 HCAPLUS
DOCUMENT NUMBER: 134:67159
TITLE: Mevalonate pathway genes involved in isopentenyl diphosphate biosynthesis in gram-positive cocci
INVENTOR(S): Brown, James R.; Gwynn, Michael; Mathie, Thomas B.; Myers, Joseph E., Jr.; Traini, Christopher M.; Van Horn, Stephanie; Wilding, Edwina Imogen
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham P.L.C.
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078935	A1	20001228	WO 2000-US17262	20000622 <--
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1999-140519P P 19990622
US 1999-146682P P 19990802
AB The invention provides mevalonate pathway genes from gram-pos. bacteria, encoded polypeptides, and methods for recombinant expression. Also provided are methods for utilizing mevalonate pathway genes, polypeptides, or antibodies for screening of antibacterial compds. The mevalonate pathway and the glyceraldehyde 3-phosphate (GAP)-pyruvate pathway are alternative routes for the biosynthesis of the central isoprenoid precursor, isopentenyl diphosphate. Genomic anal. revealed that the staphylococci, streptococci, and enterococci possess genes predicted to encode all of the enzymes of the mevalonate pathway and not the GAP-pyruvate pathway, unlike Bacillus subtilis and most gram-neg. bacteria studied, which possess only components of the latter pathway. Phylogenetic and comparative genome analyses suggest that the genes for mevalonate biosynthesis in gram-pos. cocci, which are highly divergent from those of mammals, were horizontally transferred from a primitive eukaryotic cell. Enterococci uniquely encode a bifunctional protein predicted to possess both 3-hydroxy-3-methylglutaryl CoA (HMG-CoA)

reductase and acetyl-CoA acetyltransferase activities. Genetic disruption expts. have shown that five genes encoding proteins involved in this pathway (HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase, and mevalonate diphosphate decarboxylase) are essential for the in vitro growth of Streptococcus pneumoniae under standard conditions. Allelic replacement of the HMG-CoA synthase gene rendered the organism auxotrophic for mevalonate and severely attenuated in a murine respiratory tract infection model. The mevalonate pathway thus represents a potential antibacterial target in the low-G+C gram-pos. cocci.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:454274 HCAPLUS
DOCUMENT NUMBER: 107:54274
TITLE: Inhibition of cholesterol biosynthesis by fluorinated mevalonate analogs
AUTHOR(S): Reardon, John E.; Abeles, Robert H.
CORPORATE SOURCE: Grad. Dep. Biochem., Brandeis Univ., Waltham, MA, 02254, USA
SOURCE: Biochemistry (**1987**), 26(15), 4717-22
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The conversion of mevalonate to cholesterol in rat liver homogenates (50% inhibitory concentration = 0.01-1.0 mM) is inhibited by 6-mono- (I), 6,6-di- (II), and 6,6,6-trifluoromevalonate (III), as well as 4,4-difluoromevalonate (IV). Addition of compound I, III, or IV to rat liver homogenates results in the accumulation of 5-phospho- and 5-pyrophosphomevalonate. The conversion of isopentenyl pyrophosphate to cholesterol is not inhibited by the fluorinated analogs. Thus, the decarboxylation of mevalonate 5-pyrophosphate is apparently inhibited. Rat liver homogenates catalyze the phosphorylation of I and III. The inhibition of the decarboxylation of mevalonate 5-pyrophosphate by I and III is demonstrated directly with partially purified decarboxylase. Compound I is a remarkably effective inhibitor of the decarboxylation (Ki = 10 nM). It is likely that the phosphorylated or phyrophosphorylated forms of all inhibitors tested are responsible for inhibition. A chemical method for the synthesis of mevalonate 5-pyrophosphate is also described.

L7 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:564916 HCAPLUS
DOCUMENT NUMBER: 81:164916
TITLE: Metabolism of mevalonic acid to phosphorylated intermediates in a cell-free extract from Nepeta cataria leaves
AUTHOR(S): Downing, Michael R.; Mitchell, Earl D.
CORPORATE SOURCE: Agric. Exp. Stn., Oklahoma State univ., Stillwater, OK, USA
SOURCE: Phytochemistry (Elsevier) (**1974**), 13(8), 1419-21
CODEN: PYTCAS; ISSN: 0031-9422
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cell-free extract was prepared from leaves of N. cataria plants which converted mevalonic acid to mevalonic acid phosphate, mevalonic acid pyrophosphate, and isopentenyl pyrophosphate. These enzymes were in the 30,000 g supernatant. The activities were maximal at pH 7 and the formation of mevalonic acid pyrophosphate and isopentenyl pyrophosphate reached a maximum after an incubation time of 180 min, whereas the level of mevalonic acid phosphate began to decrease after 90 min.